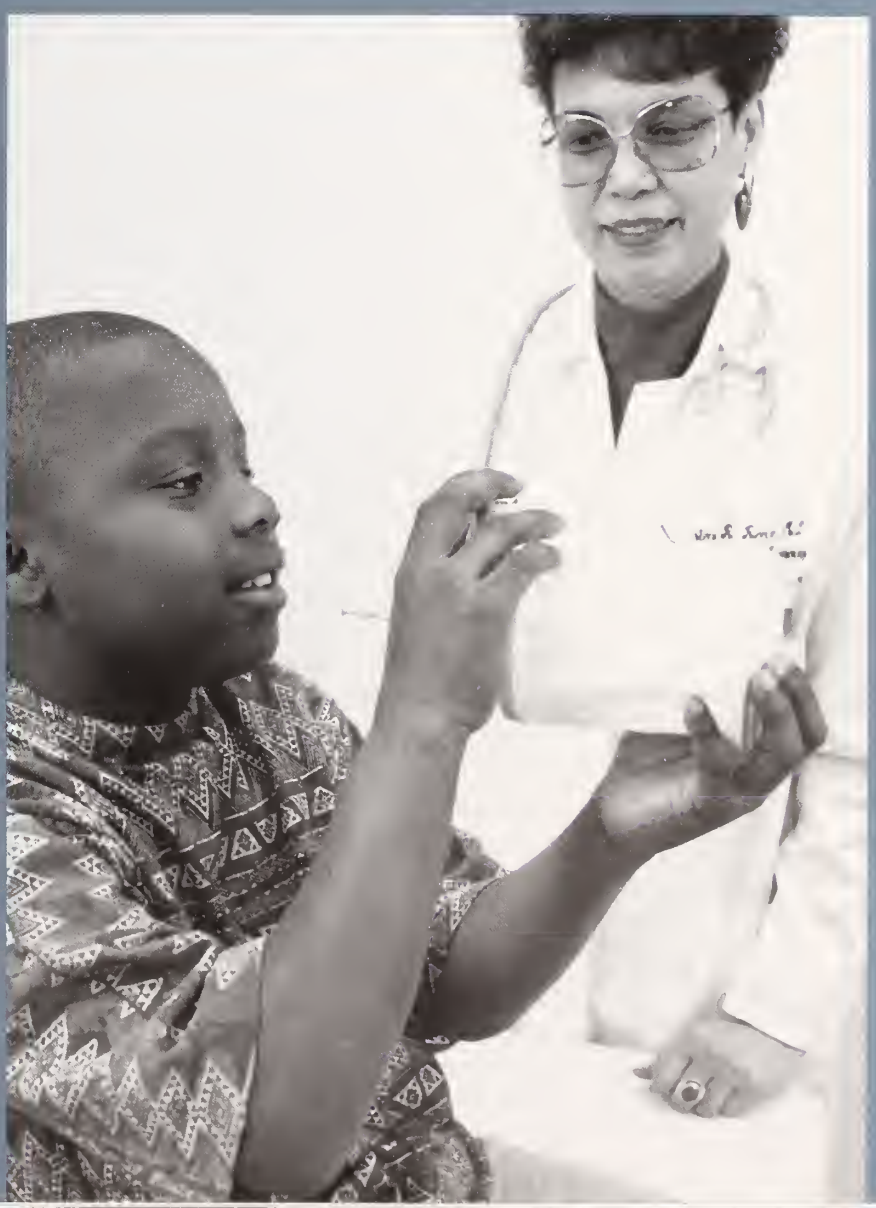
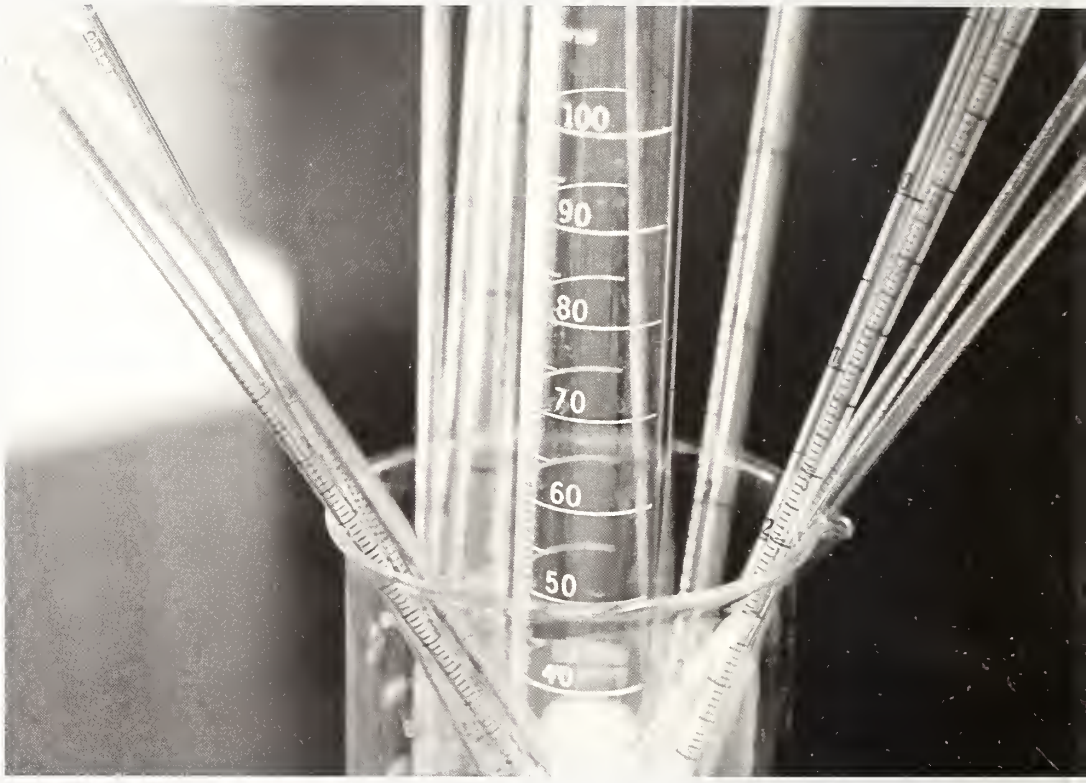
Research for the Future

National Institute of Allergy and Infectious Diseases

Asthma and Allergic Diseases

National Institutes of Health

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FOREWORD

More than 40 years ago, the United States Congress recognized the importance of studying allergic diseases and changed the name of the National Microbiological Institute to the new National Institute of Allergy and Infectious Diseases (NIAID), reflecting the growing importance of allergic diseases. Since then, NIAID has been a leader in biomedical research on allergic diseases and asthma.

Allergies are the sixth leading cause of chronic disease in the United States. Major scientific discoveries by NIAID scientists and those supported by NIAID have contributed significantly to our understanding of allergic diseases, including asthma, and have led to substantially better methods of diagnosing and treating them.

The Institute is especially concerned about the increasing asthma morbidity and mortality rates in the United States, particularly in minority populations. The seven-year-old boy pictured in this booklet represents the thousands of American inner-city minority children who have asthma, and who run a high risk of suffering from the most serious consequences of this treatable and controllable disease.

To help these children, NIAID has launched a major study in eight research institutions around the country. The scientists who are conducting the National Cooperative Inner-City Asthma Study are looking at many possible reasons why asthma is increasing and causing severe illness and death in inner-city minority children. In this creative and innovative study, they will be evaluating interventions that might be used to reverse this trend. In this booklet, we examine the challenges faced by scientists studying asthma and allergic diseases and present some of the exciting research programs that are under way to meet these challenges. We also look down the road at how research for the future may help us reach the Institute's ultimate goal—to prevent asthma and allergic diseases.

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Introduction

Allergic diseases were once brushed off as "just allergies," but we are now realizing the significant role that they play in the health and quality of life of people in this country and around the world. Among the major causes of chronic illness and disability in the United States, allergic diseases, including asthma, may affect as many as 50 million Americans, or one in five people. The economic burden of these diseases is staggering. For example, asthma was estimated to cost more than 6.2 billion health care dollars in 1990.

The National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health, stands at the forefront of scientific research on allergic and immunologic diseases. NIAID scientists and those supported by NIAID are working to prevent a broad spectrum of disorders of the immune system, including asthma and allergies.

Until prevention is possible, an intermediate goal of the Institute's research programs is to determine how allergic diseases develop and to improve diagnosis and treatment. Achieving this goal will help reduce the impact these diseases have on health and quality of life as well as reduce the economic burden imposed on individuals, families, and the health care system.

At NIAID laboratories in Bethesda, Maryland, scientists are conducting basic and clinical investigations on asthma and allergic diseases. NIAID's Division of Allergy, Immunology, and Transplantation provides research grant, contract, and cooperative agreement support to scientists at universities and other research institutions throughout the United States.

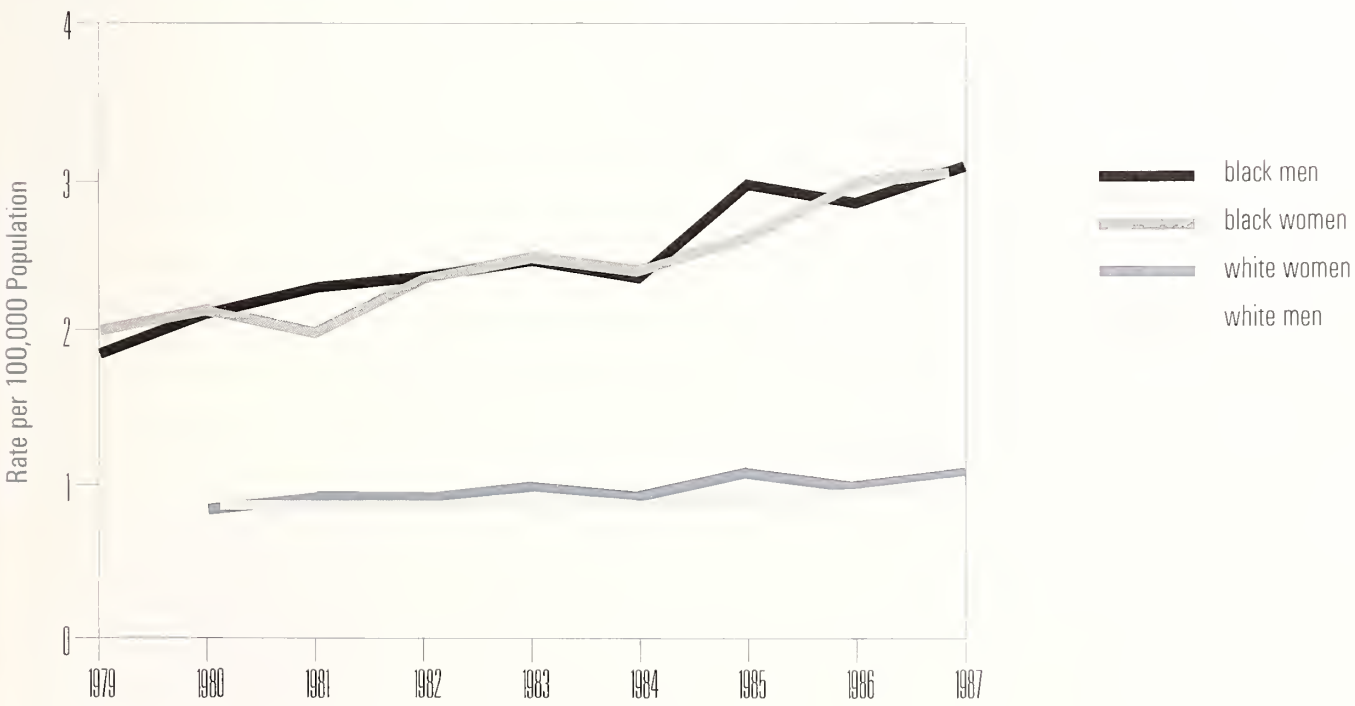
Asthma

Epidemiology

Asthma is a serious respiratory disorder that affects an estimated 10 to 15 million people and claims more than 4,000 lives in the United States each year. Despite our increased knowledge about asthma, the epidemiology of this disease in the United States presents a dismal picture. During the last decade, the prevalence of asthma cases, hospitalizations, and deaths has been increasing. For example, in 1987 twice as many children and adults, ages 5 to 34, died from asthma than in 1969.

The statistics are particularly grim in minority populations in the United States. Non-whites are almost three times as likely as whites to die from asthma. A higher percentage of African Americans have asthma than do whites. Minorities living in the inner cities seem to be at particular risk for developing asthma. For example, the rates of asthma among Puerto Rican children living in the New York City area are among the highest in the United States.

Trends in Asthma Mortality, U.S. Age -Adjusted Death Rates, 1979-1987



Source: Vital Statistics of the U.S. National Center for Health Statistics



Socioeconomics

Of the $6.2 billion spent by Americans in 1990 on asthma-related care, almost $1.6 billion was for hospital care. Another $1 billion was spent on medications to treat and control asthma symptoms. Americans also lose billions of dollars in wages because of asthma-related problems. A recent study found that school absenteeism costs an estimated $1 billion in lost pay for parents who stayed home to care for asthmatic children. Adult asthmatics who stayed home from work because of illness lost wages amounting to $850 million.

Social factors influence the rising incidence of asthma, although the magnitude of these influences has not yet been determined. Certain factors, including poverty, family problems, inadequate treatment, and lack of access to health care, probably increase an asthma patient's risk of having a severe asthma attack or, more tragically, of dying from asthma.

Although good, consistent medical attention can reduce asthma-related hospitalizations, there are 500,000 asthma-related hospital admissions each year in the United States, with a higher percentage of African Americans and Hispanics being hospitalized than whites. In New York City, for example, asthma-related hospitalizations and deaths cluster in poor, predominantly minority neighborhoods where there is often a lack of adequate primary health care.

Environmental factors can also adversely affect people with asthma. An example is indoor tobacco smoke, a well-known respiratory irritant that can cause serious problems for asthma patients. Asthmatic children with parents who smoke are at particular risk of suffering from the effects of inhaling second-hand tobacco smoke. The percentage of Americans who smoke cigarettes has been steadily decreasing, but smoking continues to remain highest among individuals who often have the least access to good health care.

Allergic Diseases

In the United States, an estimated 40 to 50 million people suffer from allergies. An estimated 33 million people have chronic sinusitis, the most prevalent allergy-related disease. Pollen allergy, commonly called hay fever, affects an estimated 19 million Americans and prompts 8 million office visits to physicians. Food allergies are believed to occur in 8 percent of children younger than 3 years old. In addition, each year billions of dollars are spent on treating allergic diseases in the United States.

When an allergic person comes in contact with an allergen (allergy-provoking substance), cells of the immune system produce an unusual class of antibody (disease-fighting protein). This class of antibody is called immunoglobulin E, or IgE, and it starts the classic allergic response. Among allergic individuals, how and to what extent their immune systems respond to a particular allergen is influenced by genetic as well as environmental factors.

While allergic reactions to airborne allergens such as pollen, mold, or dust usually cause relatively minor discomfort, sensitivity to substances such as penicillin, insect venom, or peanuts can cause anaphylaxis, a serious and potentially fatal allergic reaction. Anaphylactic reactions to penicillin are responsible for an estimated 1 to 8 deaths per million population. An estimated 1 to 2 million people experience severe allergic reactions to insect stings each year. Moreover, severe, life-threatening allergic reactions to food may occur as frequently as those to insect stings.

Research

Although a variety of therapies have been developed to treat asthma and allergies, we still do not fully understand certain critical aspects of these diseases. To develop more effective therapies and devise methods for preventing these illnesses, researchers are attempting to discern how the immune system recognizes an allergen, why people respond differently to allergens, as well as what environmental, genetic, and other factors might be responsible for allergic diseases.

Allergy to latex has become an increasingly important health problem, especially among medical personnel who wear latex gloves to reduce exposure to human immunodeficiency virus, which causes AIDS, and hepatitis B virus. Although we know proteins derived from latex cause allergic reactions, better understanding of the structure and immunologic function of these proteins would help scientists devise ways to eliminate the cause of these potentially dangerous reactions.

NIAID-funded scientists have been at the forefront of discoveries and advances in the field of allergy. They were the first to identify the IgE antibody that is the key to the allergic response. NIAID intramural investigators and NIAID-supported investigators have now identified the complete structure of the IgE receptor, the molecule on the surface of mast cells and basophils to which IgE antibodies attach. (Mast cells in the tissues and basophils in the blood are cells that together cause allergy symptoms.) Blocking the function of the IgE receptor may eventually lead to a new therapy for allergies. Investigators have studied the events that occur after allergic reactions are initiated by allergen binding to IgE antibody on mast cells and basophils. Perhaps the most important breakthrough in studying allergic reactions is the identification by NIAID investigators of the biologic events responsible for the late phase reaction (LPR). LPR usually occurs 4 to 6 hours after an allergen has entered the body. The discovery that these late reactions involve inflammatory cells and that they resemble allergic reactions has led to the recent recognition that inflammation is a central feature of allergic diseases and asthma. This knowledge has provided a significant focus to asthma research—how the inflammation is produced, how it is regulated, and how it can be prevented. In addition, NIAID investigators discovered that inhaled corticosteroids inhibit LPR. That discovery contributed to the growing use of these drugs to successfully treat both allergy and asthma.

The inflammatory process is highly complex, but the insights that have emerged highlight and expand this exciting area of research. One major key to this process is a group of powerful chemicals called cytokines, which are produced by certain cells of the immune system and which help regulate cell growth and function, including IgE antibody production and allergic and asthmatic inflammation. Substantial progress has been made recently in understanding how these chemicals are involved in most aspects of the development and function of inflammation.

Research studies have opened the door for developing promising alternative and innovative therapies such as new anti-inflammatory drugs and agents that block the actions of cytokines.

Research and the Community

National Cooperative Inner-City Asthma Study

The NIAID-supported National Cooperative Inner-City Asthma Study (NCICAS) is composed of eight units in seven cities that are studying the unusually high morbidity rates of asthma in inner-city children.

The objective of NCICAS phase I is to identify modifiable factors determining asthma severity and morbidity among inner-city children. A number of interesting findings have emerged from pilot studies. For example, allergen surveys of more than 80 inner-city homes revealed that cockroaches may be a more important trigger of asthma in this population than are house dust mites.

NCICAS is also evaluating the use of peak flow meters, plastic devices that can be used by patients at home to monitor their breathing. (Because of airflow obstruction in the lungs, asthmatics have trouble breathing air out.) From the patient's monitoring records, the doctor can tell when a person is doing well and when to take action, such as increasing medication to forestall trouble. The peak flow meter pilot studies showed that a two-week monitoring of the variability of peak air flow can be successfully and accurately carried out.

In addition, an innovative technique has been developed to measure the quality of asthma care delivered in inner-city emergency rooms.

Demonstration and Education Projects

To reduce asthma morbidity, Demonstration and Education (D & E) projects develop innovative ways to apply existing knowledge and programs. The main objectives of the projects are to teach better self-management skills to those with asthma and to increase asthma knowledge among health care providers.

Two school-based D & E projects involve new self-management skills. One project, carried out by investigators at Scripps Clinic in San Diego, California, is concerned with developing asthma intervention protocols in fourth through sixth graders in a predominantly Hispanic school district. The other, based at The Johns Hopkins University in Baltimore, Maryland, is studying new evaluation tools for asthma in 13- to 18-year-olds in a predominantly African-American school district.

In addition, a clinic-based project, a computer-driven asthma education aid for children, is in the final stages of development at Children's Hospital in Boston, Massachusetts. This program will teach asthma management skills to African-American asthma patients under age 15.

Asthma, Allergy, and Immunologic Diseases Cooperative Research Centers (AAIDCRCs)

NIAID established the Asthma, Allergy, and Immunologic Diseases Cooperative Research Centers (AAIDCRCs) to promote interaction among basic and clinical researchers and to enhance outreach and demonstration activities. These centers encourage close coordination between scientists studying fundamental concepts of immunology, genetics, biochemistry, and pharmacology and clinical investigators who treat allergic individuals. This approach will lead to both a better understanding of the complex mechanisms underlying asthma and allergies and the clinical application of this knowledge. Various allergic problems are under investigation at the AAIDCRCs: asthma; skin diseases, such as atopic dermatitis; urticaria; angioedema; and allergic reactions caused by insect stings, foods, drugs, and airborne allergens.

Studies also focus on the basic mechanisms involved in immune system function and reactions, including research on antibodies, particularly IgE, and on the inflammation-inducing chemicals released during an allergic attack.

Future

The remarkable advances during the last 10 years in our understanding of the structure and functions of the immune system are paving the way to an exciting and hopeful future for diagnosing, treating, and preventing asthma and allergic diseases.

Recent discoveries using modern molecular technology are providing a stimulus for allergic disease research. For example, scientists have developed a genetically altered mouse that produces large amounts of the cytokine interleukin-4 (IL-4). Such mice express an inflammatory response in several tissues that resembles human allergic inflammation, and they also can produce large amounts of IgE antibody. This type of approach will lead to a clearer understanding of which genes are responsible for allergic responses.

We are now beginning to understand how cytokines regulate the production of adhesion molecules that bind inflammatory cells to the sites of allergic disease, such as the nose, skin, and lungs. These and other findings suggest that molecules directed against critical targets in the allergic process–such as cytokines and adhesion molecules–may lead to a new means of therapy to better treat asthma and allergic diseases.

One of the most exciting areas of research involves unraveling the genetic mysteries of asthma and allergic diseases in conjunction with studying how allergens and other environmental factors induce these diseases. By identifying the genes responsible for them, prenatal diagnostic tests could be developed to identify persons at risk for allergic disease. This early diagnostic knowledge could be used to manipulate the environment or to start early intervention therapy, thereby eliminating or altering the severity of the disease process in these individuals. Thus, the overall quality of life would be greatly improved for these patients.

Recent studies in understanding how and why the immune systems of allergic individuals produce IgE antibodies to allergens may lead to innovative vaccine therapy. In preliminary clinical trials, scientists are evaluating an approach that could stop the immune system from responding to allergens. Called peptide-induced anergy, this process could be the "allergy shot" of the future.

Finally, researchers are working to better understand the actions of the cells and molecules associated with the inflammatory process in asthma and allergic diseases. Knowing more precisely how these cells travel to the site of inflammation in the lungs, nose, gastrointestinal tract, or skin should pave the way for new drugs that block this cascade of events.

With the quickening pace of research on asthma and allergic diseases and on the immune system, we may be able to cure–or even prevent–these chronic, often severe, and sometimes life-threatening diseases by the end of the decade.

Information Resources

Allergy and Asthma Network/
Mothers of Asthmatics, Inc.
3554 Chain Bridge Road, Suite 200
Fairfax, VA 22030
1-800-878-4403

American Academy of Allergy
and Immunology
611 East Wells Street
Milwaukee, WI 53202
1-800-822-ASMA

American College of Allergy
and Immunology
800 E. Northwest Highway
Suite 1080
Palatine, IL 60067
708-359-2800

American College of Chest Physicians
3300 Dundee Road
Northbrook, IL 60062-2340
708-498-1400

American Lung Association
American Thoracic Society
1740 Broadway
New York, NY 10019-4374
212-315-8700

Asthma and Allergy Foundation
of America
1125 15th Street, N.W., Suite 502
Washington, DC 20005
1-800-7-ASTHMA

National Asthma Education Program
Information Center
P.O. Box 30105
Bethesda, MD 20824-0105
301-251-1222

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institutes of Health

Bethesda, MD 20892

NIH Publication No. 93-493

August 1993